

Amendment to the Specification:

On page 1 of the Specification, prior to paragraph [0001] and the heading "Cross-Reference to Related Applications," please replace the title of the invention with the following amended title:

TREATMENT OR PREVENTION OF cGMP-DEPENDENT PATHOPHYSIOLOGY WITH A  
MUTANT VARIANT OF SOLUBLE GUANYLYL CYCLASE SCREENING METHOD FOR  
IDENTIFYING HEME INDEPENDENT MODULATORS OF SOLUBLE GUANYLYL CYCLASE  
(sGC) ACTIVITY USING  $\alpha\beta^{Cys105}$  MUTANT sGC

Please replace the Abstract of the Disclosure with the following amended Abstract of the Disclosure:

A method of screening a substance of interest for heme independent modulation of enzymatic activity of soluble guanylyl cyclase (sGC) is disclosed, comprising (a) obtaining  $\alpha\beta^{Cys105}$  mutant sGC enzyme; (b) determining activity of the mutant enzyme for forming cGMP from GTP in the presence of the substance of interest in a reaction medium; (c) determining activity as in step (b), except in the absence of the substance of interest; optionally, (d) including an activator other than the substance of interest in steps b) and c); e) comparing results of (b) – (d) to yield a comparison result; and f) from that value of that result, assessing activity of the substance of interest for modulating cGMP production by the mutant enzyme. Increased or decreased formation of cGMP in the presence of the substance of interest indicates activity of the substance for modulating heme independent cGMP production. Methods of using a heme-deficient mutant sGC with a substituted His105 residue, which has a high basal-specific activity and displays properties similar to NO-stimulated wild-type sGC, are disclosed. Preferred embodiments aid in the prevention and treatment of cyclic-GMP-dependent pathophysiologies, and are useful in the development of drugs that inhibit or activate sGC. Certain embodiments provide a method of treating angina and other chronic heart diseases comprising delivery of a constitutively active  $\alpha\beta^{Cys105}$  mutant gene or enzyme to an *in-vivo* cell are described.